RESEARCH REPORT
ANIMAL SCIENCE

Title: Discovery and Validation of Genetic Markers for Sow Longevity – NPB #05-107

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Industry Summary

Sow productive life, also called sow longevity, in commercial operations has drawn considerable attention over the past several years. It has been noted that there are genetic differences observed between the vast commercial lines available to the commercial producer. However, the underlying genetic causes which are responsible for these differences have not been studied until now. There has been a wealth of research on lifespan in model organisms such as the mouse, fruit fly and nematodes that show associations with certain genes to simple lifespan. The common theme between several of the genes the researchers found was that most of these genes were associated with either growth or were involved in regulating caloric intake. Our working hypothesis was that the same genes that showed association with lifespan in model organisms could also be associated in some way with sow productive life. Furthermore, we fully realized that sow productive life was a complex trait that included several components in addition to lifespan such as reproductive performance, disease resistance, feet and leg structure, as well as the many management decisions that complicate the trait.

Genetic markers were identified in twenty different candidate genes spread throughout the swine genome. All markers were originally tested in three uniquely different populations to identify their association with either longevity itself or reproduction traits. The first population consisted of approximately 1,000 commercial sows where half were older sows with 6 or more litters and the other half had less than 4 litters at the time of data collection. The second population consisted of 200 sires with a minimum of 10 daughters per sire. The reproduction records of the daughters were used to estimate the breeding values of the sires for longevity and reproduction traits. The third preliminary population consisted of reproduction records for 1,200 sows without any longevity information. All of these populations existed during the mid to late 1990s and reflected the genetics of that time period. Six genetic markers were dropped from the study after these initial populations were studied because either almost all of the animals tested had the same genotype or the marker showed no association with any longevity or reproductive trait. The fourteen remaining markers showed promise to being associated with longevity or reproductive traits, but needed to be validated in a commercial population with as current of genetics that a longevity study will allow.

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In the fall of 2005, tissue samples were acquired for DNA isolation on a fourth population to be used to validate earlier results. This population was comprised of approximately 2,000 commercial sows across three farms with half of the sows having produced at least five litters while the remaining thousand sows were gilts ranging in age from seven months to gilts about to farrow their first litter. The sows with five or more litters were selected as a more ideal or superior sow that out produced the industry average by at least 1.6 litters. The young gilts served to represent the average gilt that enters commercial production. These females were also divided such that half of the sows were PIC C22s and the remaining were PIC L42s. PigChamp^{TM} records were available to be downloaded to obtain general reproduction information and longevity records such as the number of days in the herd and the total number of parities that each female produced.

Some sows failed to have a first record, primarily due to internal id problems. From the 943 young females with PigChamp^{TM} records, 62 (6.5%) failed to produce even a single litter. A total of 13.9% of the sows that produced 1 litter failed before they produced their second litter. A total of 15.6% females that produced 2 litters failed to produce a third litter. Finally, 15.5% females that had 3 parities failed before producing their fourth litter. There are an additional 30 sows that have yet to farrow their fourth litter though they have had enough time and probably should have been culled do to reproductive difficulties. In total, 46.1% females have either dropped out or are not producing at acceptable levels before producing a fourth litter. Additionally 81 females have dropped out after producing four parities while 10 were removed after producing 5 litters. Of the 494 young females that have been removed from the farm to date, 25 sows had to be euthanized, 63 died, and 406 were culled. This means that not only did the farm lose the opportunity to get salvage value on 88 head (9.3% of the young sows), but they also had the added expense of removal on these sows.

Of the 494 young females removed to date, 56 were removed because of feed intake/body condition, 23 had gastro-intestinal issues, 24 were removed because of heart issues, 110 were removed for leg issues, 21 were culled for multiple systems failure, 36 were culled for productivity reasons, 174 were culled for reproductive issues, and the remaining 50 sows were culled for irregular reasons. The predominant reason for removal before the first parity was reproduction (n=31). The primary reasons for removal between parity one and parity two are reproduction (n=46), feet and legs (n=25), and feed intake/body condition (n=18). Likewise, the primary removal reasons between parity two and three are reproductive issues (n=28), feet and leg issues (n=30), and feed intake/body condition (n=16). Again, between parities three and four as well as between parities four and five respectively, reproductive issues (n=38 and 28) and feet and leg issues (n=29 and 20) were the primary culprits for removal reasons while for the first time sows were remove for productivity reasons (n=15 and 12).

The sows were genotyped for all genetic markers and initially were tested to see if there existed a difference in genotypic frequency between the superior older sows and the gilts. A difference in the genotypic frequency shows evidence of the marker being involved in the sows' ability to survive to parity 5. Seven genes showed a significant difference between the genotypic frequencies of the superior sows and the young gilts. These seven genes were *insulin-like growth factor binding protein 1 (IGFBP1), insulin-like growth factor binding protein 3 (IGFBP3), carnitine O-palmitoyltransferase I (CPT1A), organic cation/carnitine transporter 2* (*Solute carrier family 22 member 5*; *SLC22A5*), *angiotensin I converting enzyme* (*ACE*), and *C-C chemokine receptor 7* (*CCR7*), *tryptophanyl tRNA synthetase 2 (mitochondrial)* (*WARS2*). More precise measurements of sow longevity were also tested using PROC LIFETEST and PROC LIFEREG of SAS on the young sows. Markers were tested using these two procedures for both the sows' ability to survive in days as well as surviving to certain parities. The days that we chose to analyze were surviving to 250 days after their first service, to 500 days after first service, and to June 26, 2007 (the last time the PigChamp^{TM} records were downloaded before this publication). Additionally we tested the sows' ability of surviving to produce 1 litter, a second litter, a third litter, and a forth litter.

The PROC LIFETEST analysis showed that there was not a significant difference between the two genetic lines tested in any analysis of survival to a certain day or parity. However, there was a large and significant difference between the two farms that both contained the L42 animals. The genetic marker for *CCR7* was significantly associated with survival to parity 1 and survival to 250 days as well as tending towards significance for total active days in the herd and survival to 500 days. The genetic marker *CPT1A* was

significantly associated with surviving to parity 4 and tended towards significance for total active days in the herd. The genetic marker *MBL2* also tended towards significance for survival to parity 3, parity 4, and total active days in the herd. Additionally, *IGFPB1* and *WARS2* were also both tending towards significance for surviving to 250 days. When the effect of farm was taken into account with PROC LIFEREG, *CCR7* tended towards significance for surviving to 250 days. *MBL2* tended towards significance for both survival to parity 4 and total active days in the herd. The best results came with *CPT1A* being significantly associated with survival to parity 4 and total active days in the herd while also showing a tendency for being associated with survival to parity 3 and surviving to 500 days in the herd.

The reproduction analysis of these genes also proved to be beneficial to understanding the different roles these genes play in sow productive life. The reproductive traits that these markers were tested for included the total born in each litter and the number born alive in each litter for parities 1 through 4 individually, the number of pigs (born alive) per day of herd life, and the cumulative number of pigs (both total born and born alive) produced over the sows' lifetime. Additionally, these traits were analyzed using all of the sows' reproduction records, just the superior sows' records, as well as just the young sows' records. The genetic marker *IGFBP1* was significantly associated with several reproductive traits for the different sow groups. It was significant for the number of pigs born alive in parity 1 in the young sows with the favored genotype having 1.22 and 0.96 more pigs than the other genotypes, the total number of pigs born and the number of pigs born alive for the superior sows second litter, the total number of pigs born in parity 4 for all sows, and for the total number of live pigs over the superior sows' lifetimes with the beneficial genotype class having 2.48 more pigs than the unfavorable genotype class. After dropping the 11 genotype class from further analysis (which represented less than ten percent of the data), *MBL2* genotypes were significantly associated with differences among early reproductive traits. This genetic marker was significant for the total number of pigs born and for the number of pigs born alive in parities 1 and 2 when all sows were analyzed together with the beneficial genotype class having an additional 0.35 pigs per litter for all traits. The *CPT1A* genetic marker was significantly associated with several reproductive traits as well, especially in the later parities. The favored genotype class was associated with at least a 0.4 advantage in total number of pigs born and number of pigs born alive for all sows in parities 3 and 4. Additionally the same genotype class had an advantage of 0.005 more pigs per day on the farm for the young sows representing 1.8 more pigs per year per sow. *VDR* (missing the 11 genotype) was significantly associated with total number born in early parities and in total production for both the superior and young sow groups though identifying the favorable genotype class in not strait forward. Other markers such as *SLC22A5*, *ACE*, and *CCR7* also were associated with some reproductive trait, though they were not as consistent across sow groups or parities.

In total, several genetic markers were found to be associated with traits involved in sow productive life. These included *CPT1A*, *CCR7*, *IGFBP1*, *WARS2*, and *MBL2* which were all significantly associated with sow survival, either to a certain parity or day, when tested using extremely stringent analysis. The genetic markers *IGFBP1*, *MBL2*, *CPT1A*, *CCR7*, *SLC22A5*, and *ACE* all were significant with at least one reproductive trait. It should be noted that the favorable genotype for sow survival was the favorable genotype for reproductive traits for *CPT1A*, *IGFBP1*, and *MBL2*. However for *CCR7*, the favorable genotype for sow survival was the unfavorable genotype for reproductive traits. For *CPT1A*, *IGFBP1*, and *MBL2*, not only are these sows surviving longer, but they are simultaneously producing more pigs than their contemporaries. Though extremely positive, further research needs to be carried out on these genetic markers in other sow populations to verify the results before these markers are incorporated into selection protocols.

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Abstract

Sow productive life, also called sow longevity, has been a major concern for commercial swine operations. The average sow in U.S. commercial operations is averaging 3.4 litters before she leaves the herd. A sow must produce on average three litters before she recovers her investment cost. This small differential between when the average sow leaves the herd and when a sow has paid for herself leaves a large burden on relatively small proportion of the sow population. Even a small increase in the average number of parities that a sow produces such as one tenth of a parity could increase the revenue of commercial operation by over $15 million in the U.S. alone. While there are many different contributing factors to sow productive life, research in model organisms has showed a clear and consistent association with genes involved in growth pathways and the lifespan of these animals. Most notably are the genes involved in the insulin pathway that either reduce caloric intake or mimic the response of calorie restriction. Our hypothesis was that these same genes would also prove to be important to sow productive life, though we realize that the lifespan of simple model organisms would not be completely correlated with sow productive life, especially with the enormous demands that sows are under to continuously farrow large healthy litters. We also expanded our research to include genes that are included in nutrition, disease resistance, and reproduction. Our research on 2,000 commercial sows showed that *CPT1A, CCR7, IGFBP1, WARS2,* and *MBL2* all proved to be significantly associated with sow survival, either to a certain parity or day, when tested using extremely stringent analysis. The genes *IGFBP1, MBL2, CPT1A, CCR7, SLC22A5,* and *ACE* all were significant with at least one reproductive trait.

Introduction

The economic efficiency of swine operations is always a topic of discussion for pork producers and allied industries especially now when feed grain prices are being pushed higher as the demand for bio-fuels increases. However, many factors outside of feed prices influence the breakeven costs and thus economic efficiency for swine operations. Of those additional factors, sow herd performance is typically one of the most important categories. When producers talk about sow herd performance, most producers think about farrowing rate, pigs weaned per litter, or generally the number of pigs weaned per sow per year. We suggest that when talking about sow herd performance we need to take a more holistic view of the sow herd and incorporate sow longevity, more accurately called sow productive life (SPL) into the profit equation. The growing percentage of sows leaving the farm before they recuperate their investment cost has been increasing in recent years. These sows are being involuntarily removed from the farm for reasons such as reproductive failure, locomotion failure, and death. This early removal or premature death increases sow replacement rates and has both economic and welfare consequences to the swine industry.

PigCHAMP^{TM} records from 1998 through 2005 show an increasing trend in the death rate from 5.9% in 1998 to 8.94% in 2005 (see figure 1). The same records show that the culling rate is more variable but was at an unprecedented 51% in the most recent data available (see figure 2) (PigCHAMP^{TM}, 2006). The high culling rate seen in 2005 could be generated in part by producers taking advantage of profits and restocking their herds. High replacement rates driven by involuntary culling infer that producers are required to lower their selection intensity to maintain herd size. High replacement rates can cause a downward spiral in herd performance in systems with undersized multiplication efforts, since a heavy demand for replacement gilts may result in sub-standard gilts or gilts not properly developed entering the breeding herd. Improving SPL would help alleviate the pressures placed on multiplication herds allow for gilts to be selected more on quality than simply on quantity.

Using standard net present value calculations for a farrow to finish operation such as a purchase price of $200 per gilt, an average number born alive/litter of 10.2, 8.5 pigs sold per litter, and an average price of 44 $/CWT for market hogs, an increase in net present value of $77.38 per sow could be realized if an operation could increase litters per sow from three to four (Stalder *et al.,* 2000). Thus an increase in average parity of just one tenth of a parity would increase the profit by $0.23 for every market hog sold from the operation. For a farrow to wean operation, using the same purchase price, number born alive/litter with an average price per head of $28 for segregated early weaned (SEW) pigs, and marketing 9 pigs per litter, the net present value per sow would increase by $45.59 if a sow would have four parities instead of three (Stalder *et al*., 2003). An increase in the average parity of one tenth would increase the profit of a farrow to wean operation by $0.13 per

pig sold. Taken as a whole, a one tenth increase in average parity for the herd would raise the profit by approximately $15,000,000 per year in the U.S. alone.

Limited studies have been performed researching productive life in pigs. Most studies were only conducted up to either sow parity three (Rozeboom *et al*., 1996) or four (Moeller *et al.*, 2004) allowing for some understanding as to why sows leave the herd in early parities, but never accounting for reasons why other sows can thrive well beyond four parities. These previous studies revealed significant line interactions on sow longevity and noted that further studies should be conducted to identify the genetic mechanisms associated with sows having increased numbers of parities. More recent studies have used survival analysis to study the heritability of longevity (Serenius and Stalder, 2004) and to identify traits that are correlated (Tarres *et al*., 2006) with sow longevity. However, even the latest studies using survival analysis don't directly attack the problem in commercial crossbred populations as they focus on purebred animals.

Scientists have begun identifying genes in model organisms that play a role in the aging process and longevity itself (Hasty *et al.*, 2003; Hekimi and Guarente, 2003; Longo and Finch, 2003; Simon *et al.*, 2003; and Tatar *et al.*, 2003). Research has shown that yeast and. *C. elegans* (nematode) share a number of homologous genes in the so called "longevity pathways" and that increased longevity is often the result of inactivation of the pathways that promote growth and a reduction in oxidative damage and other forms of stress (Longo and Finch, 2003). Similar results have also been shown in the fruit fly such as mutations in the insulin / IGF-1 pathways extending lifespan. The overriding theme gathered from studying these genes is their role in reduction of caloric intake that enables animals to live longer as well as reducing susceptibility to disease in the aging process. However, some research has indicated that leaner gilts have the tendency to be removed from the herd earlier (Stalder *et al*., 2005).

The hypothesis that guides this comparative genomics research is that the similarity between the functions of certain genes in the various species studied suggests that the same genes may be associated with SPL in the pig. It is possible that genes associated with increasing simple lifespan in model organisms might not be correlated with SPL since it is more than a measure of longevity. It is also plausible that the non lean allele could be more beneficial to SPL as sows with more backfat have shown the tendency for having a longer SPL or remain in the breeding herd for a longer period of time. Additionally, other genes more specific to swine may need to be isolated and examined. Genes studied include those that function as antioxidants, are involved in reproduction, and are components of the insulin pathway that regulate food intake. The identification of molecular markers associated with the length of a sow's productive life would allow breeders to use marker assisted selection (MAS) to select individuals, based on the animal's genotype, at early ages that would have the best opportunity to remain in the herd far beyond the current average sow.

Animal Populations

We have used several distinctly different populations throughout this study in our quest to identify genetic markers associated with SPL. The first population that was analyzed consisted of approximately 1000 commercial sows where half were younger than parity four and the remaining were parity six or greater. The only phenotypic data collected on these animals were the number of parities each sow generated. The second population consisted of approximately 200 sires. The information collected and used in the analysis of this population was the EBVs based on phenotypes from a minimum of ten daughters per sire. The third population consisted of commercial females from varying parities and was primarily used to evaluate reproduction performance and thus contained reproductive data. The previous three populations were from herds composed of primarily mid 1990s genetics and no one population contained all the phenotypic records necessary to completely evaluate the candidate genes for SPL. Therefore, we felt it necessary to sample current genetics where all phenotypic records were collected from one population which would enable accurate analysis of the current state of commercial sow industry. The fourth population used here after to validate the earlier results of Mote *et al.*, 2005, consisted of 2,000 commercial sows that were sampled from a cooperator that currently has 120,000 sows in their production system. Though not ideal for a genetic study, parentage was not known on the selected females. However, it was assumed that the sample size was large enough to lessen any founder effect. The sows were from three farms with one located in Minnesota and two in Iowa and with a combined sow herd inventory of 11,400 between the three farms. The sows were evenly sampled from two genetic lines, L42 and

C22. The 1,000 L42 females were from two farms, Farm 1 and Farm 2, while all 1,000 of the C22 females were from Farm 3. Additionally, the females were subdivided into sows that are more ideal in terms of their longevity or stayability with these sows having to have produced a minimum of 5 litters and the remaining females that were sampled were all females that had just entered the farms and had yet to produce a litter. The sows that were sampled that had 5 or more litters was the group that served as our superior sows, with them having more litters than the industry average. The gilts that were sampled served to represent the unselected average gilt that enters today's commercial production systems. All gilts that were sampled were gilts in the production systems that were deemed to be acceptable replacement females by the onsite farm personnel with no preselection from us. All gilts were randomly sampled starting with the youngest group in the production line and working our way through the production barn until we obtained enough samples. The gilts ranged in age from 7 months of age to those just about to farrow. Equal numbers of superior females and young females were selected from each farm. Even with as large of a cooperator that we were working with, there system didn't contain a farm that had enough young and superior females of both genetic lines to allow sampling of both lines at one farm.

Data Collection

Ear tissue was sampled from all sows using the TypiFix™ ear tag from Agrobiogen. This system allows simultaneous identification and tissue collection to prevent sample misidentification. DNA was isolated from tissue samples using the Nexttec™ DNA isolation system (Nexttec GmbH Biotechnologie) adhering to the manufacture's protocol. PigCHAMP™ records were obtained throughout the research trial by downloading the farms database and corresponding the sows' farm identification number with the TypiFix™ ear tag. Of the wealth of information that is available from PigChamp, the records that we felt were most informative to us and were therefore collected were the reproductive information for all parities that the sows had and the general longevity information. The data that we collected regarding the longevity information were the sows' entry date into the herd, their removal date, removal parity, removal type (cull, death, or destroyed) removal reason, lifetime nonproductive days, and total days in the herd. The reproductive data that were collected included farrowing dates, gestation length, total born, number born alive, stillborn, mummies, total pigs weaned, lactation length, and wean to first service interval (WFSI) for each parity that the sow produced. SAS PROC UNVARIATE was used to generate the means, standard deviations, and extreme values observed (see table 1). The extreme data points were flagged as outliers that might represent possible false data. All data points were hand checked to ensure that the data were within the realistic bounds for the given trait. For WFSI, all values over 42 days were deleted as they represented sows that were either extremely hard to detect heat on or they were simply lost in the farm system. Arguably, the sows whose WFSI was between 21 and 42 days could have been censored as well as it could have been human error in heat detection, but we felt that these sows needed to be included as either they didn't actually come into heat during the first 21 days or they did not express estrus strong enough to be detected. Gestation lengths were calculated from the date first bred until the farrowing date. All gestation lengths were also right censored at 121days. Those dates above 121 days were either from when the sow was bred during the next cycle (data we did not have), the observation was suspected of being flawed, or it was not possible to tell if the sow farrowed either extremely late (over 121 days) from the first breeding date or extremely early (less than 107days) from being bred if she came back in heat.

Of the 1,000 young females that were tagged, there was substantially more lost data than ideal. A total of 57 records were omitted from use in any reproduction data due to sow identification issues primarily caused by multiple sows having the same farm ID or entry/removal date not matching their specified age group. The sows whose reproduction records were omitted because of multiple sows having the same farm ID could still be used in tests where specific reproduction records were not necessary to contrast between the old and young groups. Of the 1,000 older females, 38 records were also omitted because of sow identification issues.

Statistical analysis

To determine if the genetic markers were associated with the longevity side of sow productive life, three different methods were utilized. When the project was in the initial stages, sows' genotypes were analyzed

using Fisher's exact test to identify if there was a significant deviation in frequency for the gene markers between the select and unselected sow groups for sows remaining in the herd until the fifth parity. After the unselected young sows were given the opportunity to produce four parities, we proceeded to analyze SPL on only the young unselected females using two different methods of survival analysis. The first of these methods was the PROC LIFETEST procedure of SAS. This procedure simultaneously computes significance for three distinctly different calculations (Log-Rank, Wilcoxon, and -2Log(LR)) for survival to a set point. The other method of survival analysis was the PROC LIFEREG procedure of SAS. This survival analysis allows for multiple fixed and random effects to be fitted into the model. For this analysis, genotype and farm were included as fixed effects. For both the PROC LIFETEST and PROC LIFEREG procedures, the genotypes were analyzed to determine if they were significantly associated with survival to parity1, parity 2, parity 3, parity 4, 250 days post first service, 500 days post first service, and total days post service.

The PROC MIXED procedure of SAS was also used to determine genotype effects on the reproductive traits that we analyzed. We analyzed the select and unselect groups individually as well as a combined analysis. We used genotype, line/farm, and maximum number of parities as fixed effects and also tested to see if there were any age by genotype or farm by genotype interactions. The traits studied were total number of pigs born per litter and number of pigs born alive per litter. Each parity was tested individually. Additionally, genetic markers were tested for associations with the total number of pigs born alive over the sows' lifetime as well as for the number of pigs per day since first service.

Results

From the 943 young females with reproduction records, 62 (6.5%) failed to produce even a single litter. This number was surprisingly higher than expected since all the females had passed the farm personnel's qualifications as being an acceptable replacement female and many of the young females were tagged after they were considered bred. Had all females in this group been fresh replacement gilts instead of some gilts about to farrow, this number of gilts that failed to produce a single litter could have been much higher. This group is of the highest importance to minimize since they represent a high negative return on investment having the expenses of their replacement cost, feed cost, semen cost, possible removal cost, and their facilities cost while having at best a minimal cull value in return. A total of 123 of the 881 (13.9%) sows that produced 1 litter failed before they produced their second litter. A total of 119 of the 758 (15.6%) females that produced 2 litters failed to produce a third litter. There are 2 females that have had 2 litters but haven't had their third litter yet, though they have ample time to produce their third litter. Both of these sows have extremely large Lifetime Non Productive Days indicating they either didn't settle when farm personnel thought they were or they aborted without being noticed. Either way, they were not caught by the farm personnel for quite some time. A total of 99 of the 637 (15.5%) females that had 3 parities failed before producing their fourth litter. There are an additional 30 sows that have yet to farrow their fourth litter though they have had enough time and probably should have been culled do to reproductive difficulties. A total of 435 (46.1%) females have either dropped out or are not producing at acceptable levels (2 females haven't produced a third litter and 30 haven't produced a fourth litter) before producing a fourth litter. Additionally, 81 females have dropped out after producing four parities while 10 were removed after producing 5 litters.

Of the 494 young females that have been removed from the farm to date, 25 sows had to be euthanized, 63 died, and 406 were culled. This means that not only did the farm lose the opportunity to get salvage value on 88 head (9.3% of the young sows), but they also had the added expense of removal on these sows. Most (n=18) of the young sows that had to be euthanized were done so because of leg issues. A total of 20 of the 63 sows that died were listed as having heart failure as the reason. This is interesting because these were young sows and one would not expect so many young sows to be culled for this reason.

Of the 494 young females removed to date, 56 were removed because of feed intake/body condition, 23 had gastro-intestinal issues, 24 were removed because of heart issues, 110 were removed for leg issues, 21 were culled for multiple systems failure, 36 were culled for productivity reasons, 174 were culled for reproductive issues, and the remaining 50 sows were culled for irregular reasons. The predominant reason for removal before the first parity was reproduction (n=31). The primary reasons for removal between parity one and parity two are reproduction (n=46), feet and legs (n=25), and feed intake/body condition (n=18). Likewise, the

primary removal reasons between parity two and three are reproductive issues (n=28), feet and leg issues (n=30), and feed intake/body condition (n=16). Again, between parities three and four as well as between parities four and five respectively, reproductive issues (n=38 and 28) and feet and leg issues (n=29 and 20) were the primary culprits for removal reasons while for the first time sows were remove for productivity reasons (n=15 and 12).

For the sows in the older group (n=972), 886 were culled, 46 (4.7%) died and 16 had to be put down. This leaves 24 of the older sows still producing within the system. 79 of the older sows were removed because of feed intake/body condition, 25 were culled because of gastro-intestinal problems, 9 for heart related issues, 71 were removed because of feet and leg issues, 457 were culled simple because of old age/ parity, 102 were culled because of productivity, 116 were culled because of reproduction issues, no reason for culling was listed for 49 sows, and the remaining 40 were culled for irregular issues. We did not analyze the removal reasons for the older sows by parity since we had a large range in parity distribution (from 5 to 13) when samples were collected on older sows.

The sows were genotyped for all genetic markers and initially were tested to see if there existed a difference in genotypic frequency between the superior older sows and the gilts. A difference in the genotypic frequency provides evidence of the marker being involved in the sows' ability to survive to parity 5. Seven genes showed a significant difference between the genotypic frequencies of the superior sows and the young gilts. These seven genes were *insulin-like growth factor binding protein 1 (IGFBP1), insulin-like growth factor binding protein 3 (IGFBP3), carnitine O-palmitoyltransferase I (CPT1A), organic cation/carnitine transporter 2* (*Solute carrier family 22 member 5*; *SLC22A5*), *angiotensin I converting enzyme* (*ACE*), and *C-C chemokine receptor 7* (*CCR7*), *tryptophanyl tRNA synthetase 2 (mitochondrial)* (*WARS2*).

The young unselected sow group was then used to test for survivability using the PROC LIFETEST and PROC LIFEREG procedures. The PROC LIFETEST analysis showed that there was not a significant difference between the two genetic lines tested in any analysis of survival to a certain day (see figure 3) or parity (not shown). However, there was a large and significant difference between the two farms that both contained the L42 animals (see figures 4 and 5). The genetic marker *CCR7* was significantly associated with survival to parity 1 (Log-Rank P = 0.0367 and Wilcoxon P = 0.0309) (see figure 6) and survival to 250 days (Log-Rank P = 0.003 and Wilcoxon P = 0.0026) (see figure 7) as well as tending towards significance for total active days in the herd and survival to 500 days. The genetic marker *CPT1A* was significantly associated with surviving to parity 4 (Log-Rank P = 0.025) (figure 8) and tended towards significance for an association with total active days in the herd (figure 9*)*. The *Mannose-binding lectin (protein C) 2* (*MBL2*) marker tended towards significance for an association with survival to parity 3, parity 4, and total active days in the herd. Additionally, *IGFPB1* and *WARS2* were also both tended towards significance for associations with surviving to 250 days. When the effect of farm was taken into account with PROC LIFEREG, *CCR7* tended towards significance for an association with surviving to 250 days. *MBL2* tended towards significance for both an association with survival to parity 4 and total active days in the herd. The best results came with *CPT1A* being significantly associated with survival to parity 4 (P = 0.0173) and total active days in the herd (P = 0.0221) while also showing a tendency for being associated with survival to parity 3 and surviving to 500 days in the herd.

The reproduction analysis of these genes also proved to be beneficial to understanding the different roles these genes play in sow productive life. The reproductive traits that these markers were tested for included the total born in each litter and the number born alive in each litter for parities 1 through 4 individually, the number of pigs (born alive) per day of herd life, and the cumulative number of pigs (both total born and born alive) produced over the sows' lifetime. Additionally, these traits were analyzed using all of the sows' reproduction records, just the superior sows' records, as well as just the young sows' records. As with the heavy use of cross fostering on these farms, we did not analyze the total number of pigs weaned per litter. The *IGFBP1* genetic marker was significantly associated with several reproductive traits for the different sow groups. It was significant for the number of pigs born alive in parity 1 in the young sows with the favored genotype having 1.22 and 0.96 more pigs that the other genotypes, the total number of pigs born and the number of pigs born alive for the superior sows second litter, the total number of pigs born in parity 4 for all sows, and for the total number of live pigs over the superior sows' lifetime with the beneficial genotype class having 2.48 more pigs

than the unfavorable genotype class. After dropping the 11 genotype class from further analysis (which represented less than ten percent of the data), *MBL2* was significantly associated with early reproductive traits. It was significant for the total number of pigs born and for the number of pigs born alive in parities 1 and 2 when all sows were analyzed together with the beneficial genotype class having an additional 0.35 pigs per litter for all traits. *CPT1A* was significantly associated with reproductive traits as well, especially in the later parities. The favored genotype class was associated with at least a 0.4 advantage in total number of pigs born and number of pigs born alive for all sows in parities 3 and 4. Additionally, the same genotype class had an advantage of 0.005 more pigs per day on the farm for the young sows representing 1.8 more pigs per year per sow. *Vitamin D receptor* (*VDR*) was significantly associated with larger litters in early parities and in total production for both the superior and young sow groups though identifying the favorable genotype class in not strait forward. Other markers such as *SLC22A5*, *ACE*, and *CCR7* also were associated with some reproductive trait, though they were not as consistent across sow groups or parities. For complete reproductive analysis see table 2.

Discussion

As seen from previous research, the primary culprit for the young sows leaving the farm early was reproductive failure. Very few of the females in the young group were voluntarily culled for poor performance before they reached parity 4 (1.1%). This leads us to believe that either most females are producing at acceptable levels or that if they aren't producing at the desired levels then they are simply around to fill crate space. From analyzing the difference between the reproduction records of the sows that produced at least five litters to the young females, it is easily seen that the sows that survived to parity five also out performed the young unselected females in the number of pigs born alive in the first four parities as well as breed back quicker after each litter. It should also be noted that a large portion of the superior sows did not fail, but were merely culled because of old age though they maintained superior reproductive performance. We feel that these truly superior sows should be given the opportunity to fail, which could allow the management the chance to cull some of the younger sows that are not producing up to par.

Unfortunately, the use of differences in genotypic frequencies between the superior and the young unselected group should probably not be used as a test for survival when only subsets of a population are sampled. Differences in genotypic frequencies alone do not account for other fixed effects and may be unreliable indicators of longevity or SPL. We realize that both PROC LIFETEST and PROC LIFEREG are extremely stringent in the methods and test used to find significant differences. Analysis with PROC LIFETEST and PROC LIFEREG more clearly reveal which genotype is actually the preferred genotype for survival. The best example of this is shown by the genetic marker *CCR7*. While it was shown to be significant using all methods, there were differences in which genotype is actually the best for survival to later parities. Looking at the differences in the genotypic frequencies between the superior and the young unselected sows, the 11 genotype appeared to be the best for survival. However, when the young unselected group was tested using survival analysis, the 22 genotype was actually favored.

In total, several genetic markers were found to be associated with traits involved in sow productive life. The markers *CPT1A*, *CCR7*, *IGFBP1*, *WARS2*, and *MBL2* all proved to be significantly associated with sow survival, either to a certain parity or day, when tested using extremely stringent analysis. The markers *IGFBP1*, *MBL2*, *CPT1A*, *CCR7*, *SLC22A5*, and *ACE* all were significant with at least one reproductive trait. It should be noted that the favorable genotype for sow survival was the favorable genotype for reproductive traits for *CPT1A*, *IGFBP1*, and *MBL2*. However for *CCR7*, the favorable genotype for sow survival was the unfavorable genotype for reproductive traits. Why this is the case in unknown and needs further study. For the genetic markers *CPT1A*, *IGFBP1*, and *MBL2*, not only are these sows surviving longer, but they are simultaneously producing more pigs than their contemporaries. Though these results are on average very useful, further research needs to be carried out on these genetic markers in other sow populations to verify the results before these markers are incorporated into selection protocols.

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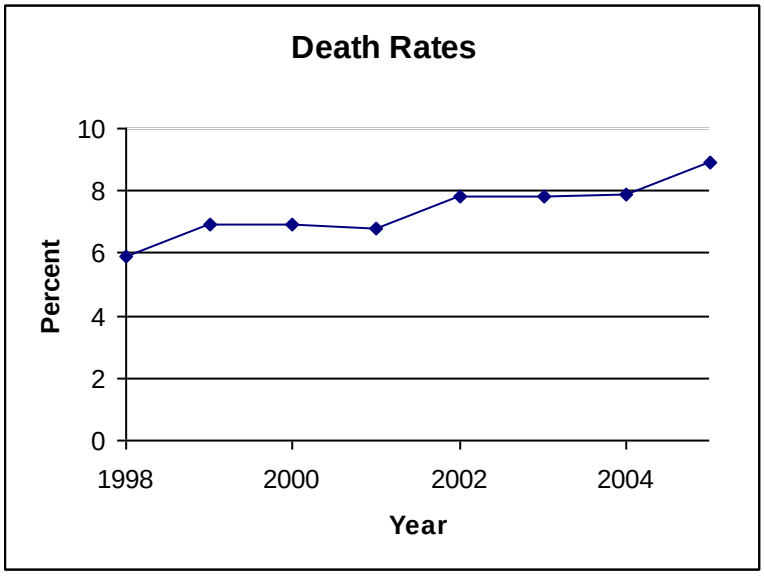

Figure 1.
This figure shows the increasing death rates in commercial swine operations using PigCHAMP^{TM} since 1998.

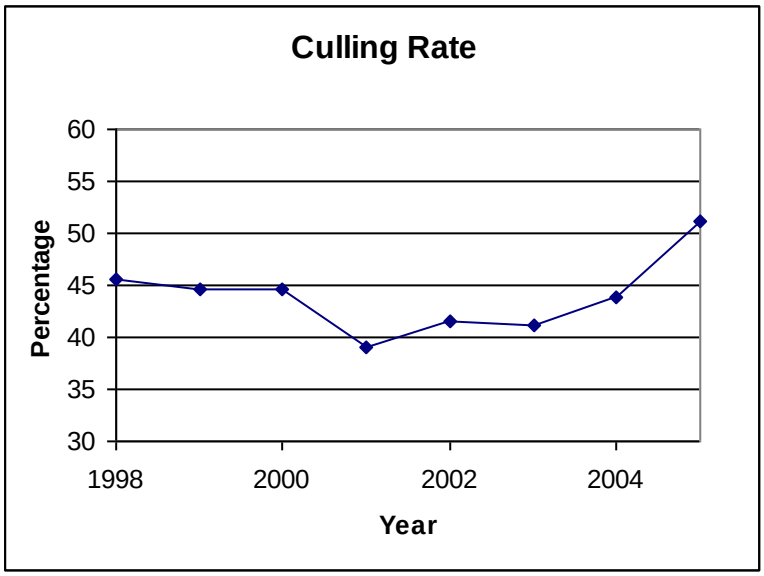

Figure 2.
This figure shows the variable culling rate in commercial swine units since 1998.

Animal Group	Trait	Parity	N	Mean	Standard Deviation
Young Sows	Total Born	1	881	11.95	3.21
Superior Sows	Total Born	1	972	12.33	3.11
Young Sows	Total Born	2	758	12.3	3.36
Superior Sows	Total Born	2	972	12.33	3.10
Young Sows	Total Born	3	637	13.04	3.63
Superior Sows	Total Born	3	972	13.2	2.91
Young Sows	Total Born	4	508	13.09	3.57
Superior Sows	Total Born	4	972	13.29	2.96
Young Sows	Total Born	all	881	12.33	2.56
Superior Sows	Total Born	all	972	12.16	1.78
Young Sows	NBA	1	881	10.75	3.21
Superior Sows	NBA	1	972	11.26	3.00
Young Sows	NBA	2	758	11.11	3.08
Superior Sows	NBA	2	972	11.46	3.07
Young Sows	NBA	3	637	11.67	3.34
Superior Sows	NBA	3	972	11.99	2.84
Young Sows	NBA	4	508	11.64	3.42
Superior Sows	NBA	4	972	11.96	2.86
Young Sows	NBA	all	881	10.99	2.56
Superior Sows	NBA	all	972	11.17	1.67
Young Sows	WFSI	1	854	7.00	5.72
Superior Sows	WFSI	1	969	6.32	4.96
Young Sows	WFSI	2	692	5.85	4.69
Superior Sows	WFSI	2	965	5.89	4.03
Young Sows	WFSI	3	575	5.34	4.14
Superior Sows	WFSI	3	960	5.42	3.43
Young Sows	WFSI	4	416	5.29	3.75
Superior Sows	WFSI	4	968	5.30	3.6
Young Sows	WFSI	all	859	6.41	4.11
Superior Sows	WFSI	all	972	5.51	1.79

Table 1.

This table shows the averages for both the Superior and Young sows for the more important reproductive traits analyzed. It should be noted that the Superior sows were in fact superior in terms of the reproductive traits when analyzed at the same parity.

NBA= number born alive; WFSI = wean to first service interval

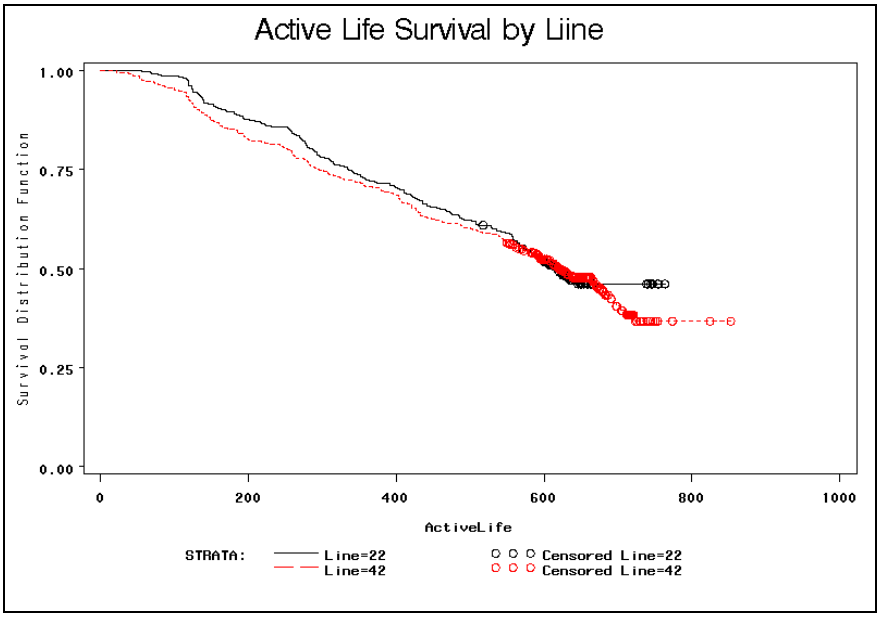

Figure 3.
This figure shows that there is not significant difference between the two genetic lines for Active Life measured in days since their first attempted breeding date. Most of the data past roughly 500 days is censored data and should not be judged by the naked eye for significance.

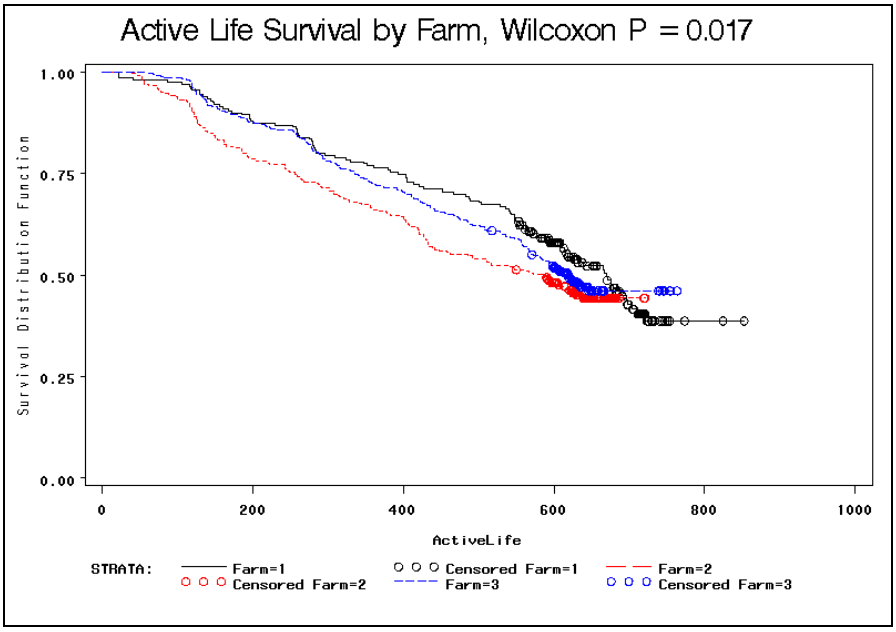

Figure 4.
This figure shows the significant difference that Farm 2 had in days of Active Life compared to the other two farms. This difference is not a line effect as Farm 1 also has the L42 animals. This simply shows the large effects that management has on sow survival.

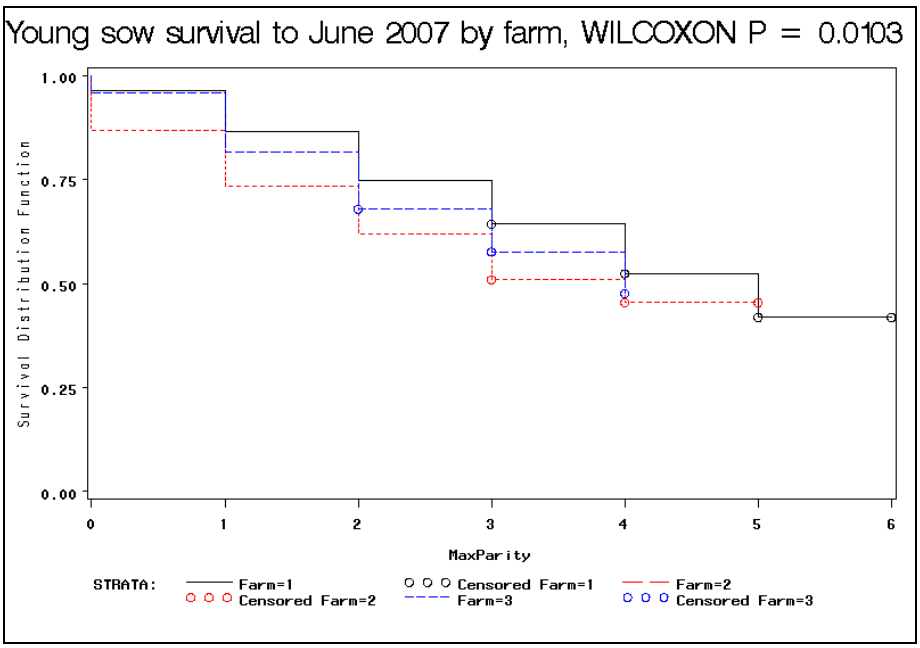

Figure 5.

This figure also shows the difference that Farm 2 had in sow survival, but is shown in survival to certain parities. It is easy to see that a substantial number of females are lost from Farm 2 before they even produce a litter.

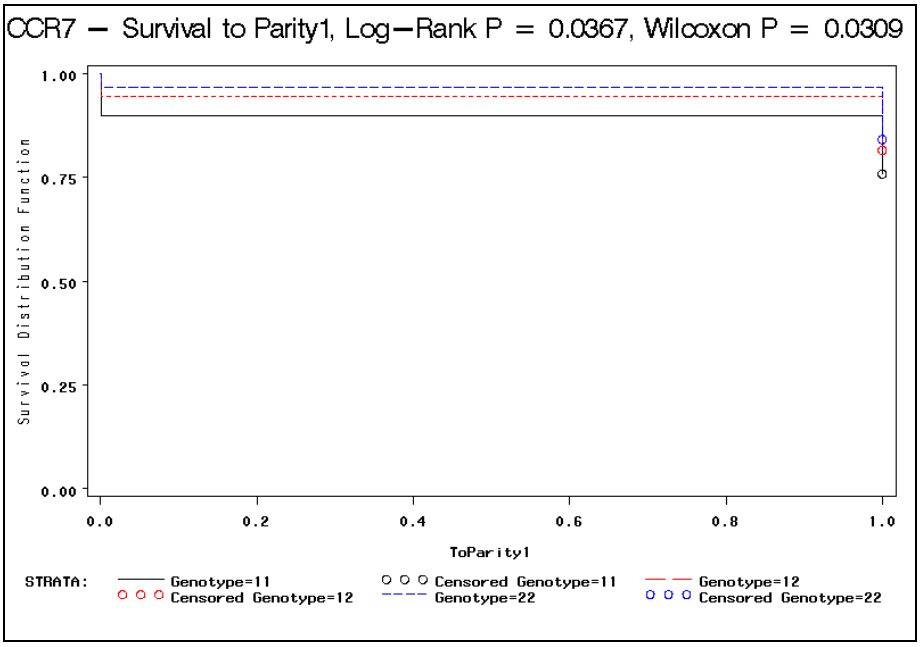

Figure 6.

This figure shows the significant difference between the genotypes for CCR7. The unfavorable genotype for survival to parity 1 is the 11 genotype.

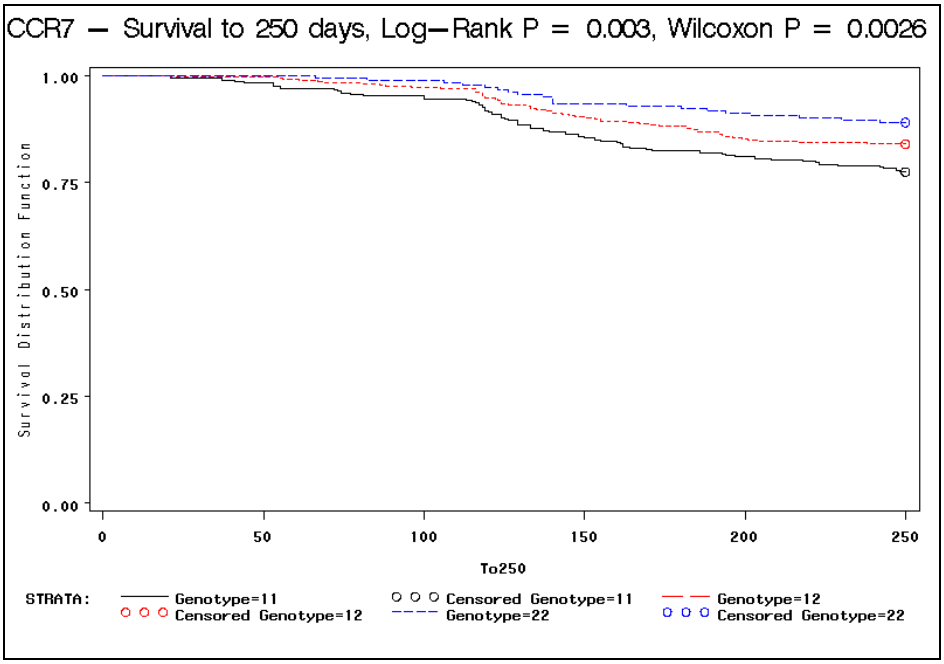

Figure 7.
This figure shows the significant differences in survival to 250 days after the gilts were first bred. Again, the 11 genotype is the unfavorable genotype for survival.

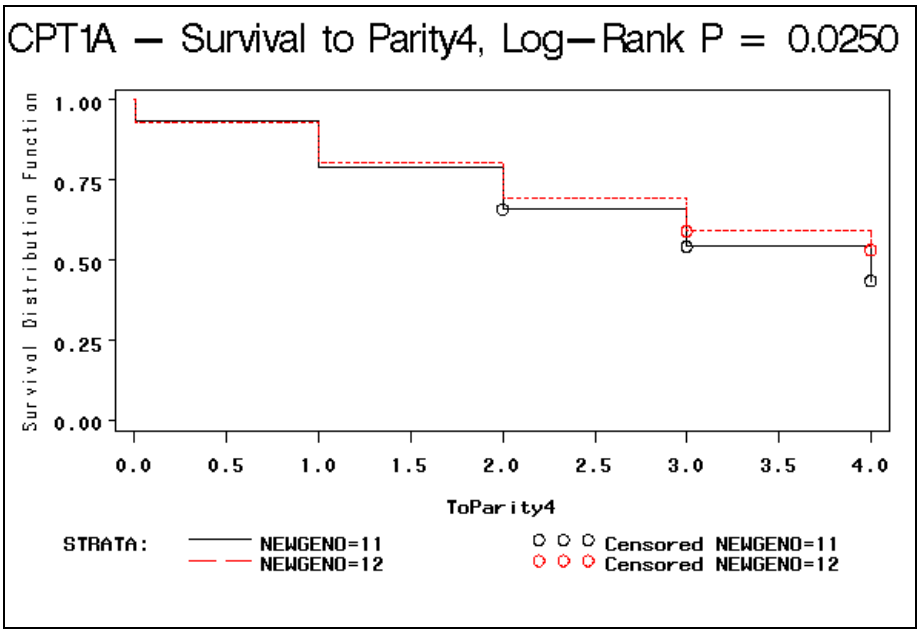

Figure 8.
This figure show the significant difference between the 11 and 12 genotype classes. It should be noted that the 22 genotype because it represented a very low percentage of the data and possessed large standard errors. However, the 22 genotype was superior to both the 12 and 11 genotype classes.

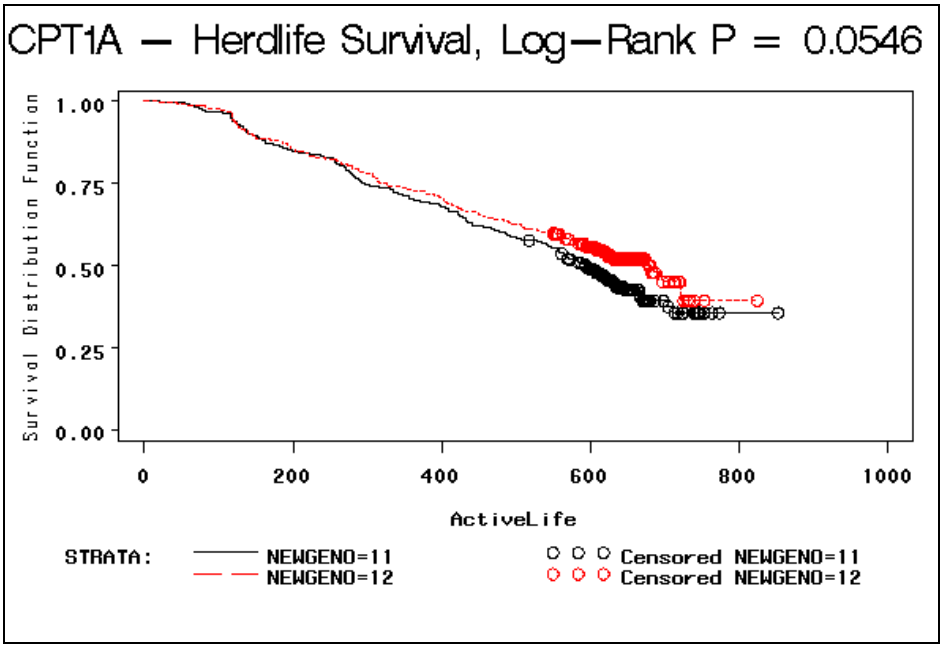

Figure 9.
This figure shows the tendency for the 12 genotype to be favored over the 11 genotype. Again the 22 genotype was dropped from this analysis.

Gene	Group	Trait	Parity	Pr > F	11 Genotype (SE)	12 Genotype (SE)	22 Genotype (SE)
ACE	All Sows	Total NBA	Lifetime	0.0012	61.92 (0.76)	63.11 (0.38)	64.77 (0.44)
CCR7	Old Sows	NBA	4	0.0479	12.46 (0.15)	12.11 (0.16)	11.34 (0.48)
CPT1A	Young Sows	Pigs per active day of life	Lifetime	0.0463	0.068 (0.0010)	0.071 (0.0010)	0.073 (0.0028)
CPT1A	All Sows	Total born	3	0.0308	13.01 (0.14)	13.47 (0.13)	13.67 (0.31)
CPT1A	Old Sows	Total born	3	0.0283	13.17 (0.18)	13.30 (0.14)	14.05 (0.28)
CPT1A	All Sows	NBA	4	0.0362	11.75 (0.14)	12.25 (0.13)	12.21 (0.30)
CPT1A	Old Sows	NBA	4	0.0134	11.87 (0.17)	12.52 (0.13)	12.31 (0.27)
CPT1A	All Sows	Total born	4	0.0261	13.02 (0.15)	13.58 (0.13)	13.48 (0.32)
CPT1A	Old Sows	Total born	4	0.0191	13.10 (0.17)	13.71 (0.14)	13.78 (0.28)
IGFBP1	Young Sows	NBA	1	0.0362	10.64 (0.20)	10.90 (0.19)	11.86 (0.42)
IGFBP1	Old Sows	NBA	2	0.0375	11.24 (0.19)	11.88 (0.16)	11.80 (0.27)
IGFBP1	Old Sows	Total born	2	0.0164	12.05 (0.20)	12.79 (0.16)	12.61 (0.28)
IGFBP1	All Sows	Total born	4	0.0151	13.05 (0.16)	13.64 (0.14)	13.04 (0.27)
IGFBP1	Young Sows	Total born	4	0.0502	12.98 (0.30)	13.70 (0.28)	12.19 (0.63)
IGFBP1	Old Sows	NBA	Lifetime	0.0432	86.69 (0.78)	89.09 (0.64)	89.17 (1.12)
MBL2	All Sows	Total born	1	0.0298	11.86 (0.24)	12.24 (0.10)	12.58 (0.14)
SLC22A5	All Sows	NBA	4	0.0439	12.15 (0.36)	11.73 (0.13)	12.19 (0.12)
SLC22A5	Young Sows	NBA	4	0.0425	12.55 (0.94)	11.34 (0.26)	12.18 (0.22)
SLC22A5	All Sows	Total born	4	0.0302	13.28 (0.37)	13.06 (0.14)	13.59 (0.13)
VDR	Young Sows	Total born	2	0.0409	NA	13.00 (0.26)	12.36 (0.16)
VDR	Young Sows	Total NBA	Lifetime	0.0464	NA	37.55 (0.52)	36.34 (0.31)

Table 2.
This table shows all the traits that were significantly associated with each genetic marker.